consisting of epithelial cells, keratinocytes, embryonic cells, fetal cells, liposomes and combinations thereof.

REMARKS

Claims 1 - 20 are pending. The claims have been amended to narrow the issues under consideration, and to more clearly and definitely claim the subject matter Applicants regard as their invention, without prejudice to the prosecution, of subject matter cancelled by amendment, in other patent applications. Applicants attach, on a separate sheet, a version of the claims marked to show amendments.

The amendments do not constitute new matter. In particular, support for the amendments relating to thrombocyte activating substances is found in the instant specification at page 2 lines 11-14, and support for release "over an extended period of time" is found at page 4 lines 11-15 and in the results of working example 5 described at page 9, lines 8-14. The amendment to claim 4, with regard to particular biomaterials, is supported by the instant specification at page 7 lines 5-9 and page 7 lines 20-22. Copies of these pages, highlighted to show the cited text, are attached hereto

In the Official Action dated May 3, 2001, the claims were rejected under 35 U.S.C. § 112 and §102. For reasons to be set forth below, these rejections should not be reapplied.

1. The Claims Are Not Indefinite

Claims 1-20 are rejected under 35 U.S.C. §112 as indefinite for the recitation "deep-frozen".

Applicants have amended the claims to delete "deep" from the phrase. As Applicants argued in a response to a previous Official Action, a person skilled in the art would understand the meaning of "frozen".

2. The Claims Are Not Anticipated

Claims 1, 4, 6 and 10 are rejected under 35 U.S.C. §102(b) as anticipated by Read et al., United States Patent No. 5,902,608 ("Read"). According to the Examiner, Read teaches a sterile surgical composition comprising thrombocytes containing growth factor, which may be prepared by deep-freezing and/or lyophilization.

Applicants assert that the amended claims are not anticipated by Read. In particular, the claims have been amended to reflect an important component of non-limiting embodiments of the invention - the use of a thrombocyte activating stimulus. Applicants invite the Examiner's attention to the instant specification at page 2, lines 11-14, which explain that such a stimulus is required for the release of stored growth factors. Further, Applicants invite the Examiner's attention to the working examples of the application which demonstrate the use of such a stimulus, at page 8 lines 27-29 (the bottom three lines of the page) and at page 10, lines 5-9.

Read makes no teaching of the adjunct use of a thrombocyte activating stimulus, either in embodiments relating to thrombocytes for infusion into a host or as applied to a wound. With regard to this latter embodiment, Applicants invite the Examiner's attention to Read at column 3 line 56 through column 4 line 67 and working example 10 at column 11 line 45 through column 12 line 32. The disclosure neither expressly nor impliedly teaches or even suggests the adjunct use of a thrombocyte activating substance.

Accordingly, Read does not anticipate the claims, so that this rejection should not be reapplied.

3. The Claims Are Not Obvious Over The References

Claims 1-20 are rejected under 35 U.S.C. §103(a) as obvious over Read and Patat et al. (United States Patent No. 5,589,462, "Patat", of record) in view of Delmas (United States Patent No. 5,618,663, "Delmas", of record) and Dimoudis et al. (1996, CA Abstract, AN 1996:313895, "Dimoudis", of record).

According to the Examiner, (i) Read teaches a sterile surgical composition comprising thrombocytes containing growth factor, where the thrombocytes may be prepared by lyophilization or deep-freezing; (ii) Patat teaches a product for topical

application to wounds comprising frozen growth factor-containing thrombocytes; (iii) Delmas teaches that it is necessary to inactivate viruses in therapeutic thrombocyte products; and (iv) Dimoudis teaches the utility of epithelial cells in wound healing compositions. The Examiner states:

> A person of ordinary skill in the art would have been motivated to make a sterile platelet factor enriched thrombocyte composition[] with inactivation of viruses and by the addition of other known wound healing components such as epithelial cell[s] because both using thrombocytes or the growth factor extract from the thrombocytes for wound healing is known. The inactivation of viruses is well known to be necessary for any topical wound healing composition to avoid any possible transmission of disease. The addition of epithelial cells is seen to be obvious since epithelial cells are known to be useful in wound healing composition[s]. The combination of the above known ingredients is obvious because it is prima facie obvious to combine two or more components each of which is taught in the prior art to be useful for [the] same purpose in order to form a third composition that is to be used for the very same purpose; [the] idea of combining them flows logically from their having been individually taught in [the] prior art . . .

Applicants assert that the claims are not rendered obvious by any of the cited references. As set forth in the preceding section, Read does not teach the use of a thrombocyte activating stimulus. Applicants submit for the Examiner's consideration that the use of this activating substance may explain why much lower amounts of thrombocytes are required by the method of the present invention, relative to Read; as shown in the working examples of the pending application, a thrombocyte preparation having 6×10^5 thrombocytes per microliter (page 7, lines 7-8) was used in an amount of 200 microliters per square centimeter, or 1.2×10^8 thrombocytes/square centimeter. In contrast, Read teaches that at a minimum, 5×10^8 thrombocytes and at most 10^{10} thrombocytes per square inch should be used (Read at column 4 lines 18-24). Read may require more thrombocytes because an activating stimulus is not used.

Further, Read teaches against the use of thrombocyte fragments encompassed by the pending claims, stating "[b]lood platelet preparations for use in preparing pharmaceutical formulations should be essentially free of extraneous matter, particularly lysed blood platelets".

As set forth in Applicants' Amendment dated February 15, 2001, Patat does not relate simply to frozen platelets, but rather to a cryoprecipitate prepared under extremely specific temperature conditions whereby sequential freezing and thawing produces a solid fraction (hence *precipitate*).

Almost the opposite of Patat, Delmas teaches viral inactivation of a supernatant containing soluble growth factors that are not sedimentable by centrifugation. Delmas, contrary to the present invention, teaches against compositions comprising thrombocytes. Applicants would argue that because Delmas teaches against the use of thrombocytes, there is no basis to combine its teachings with the other references.

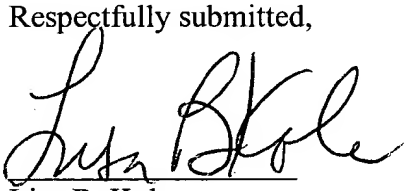
In any case, the disclosures of Read, Patat, Delmas and Dimoudis fail to suggest the elements of the claimed invention. Read discloses a composition of fixed, dried thrombocytes, but not an activating stimulus; Patat teaches a cryoprecipitate, Delmas teaches a filtrable supernatant and Dimoudis teaches the use of epithelial cells in wound healing preparations. None of these teachings, considered separately or in combination, would suggest to the skilled artisan the use of a composition of thrombocytes or thrombocyte fragments, to which is added a thrombocyte activating stimulus.

Accordingly, the rejection under 35 U.S.C. §103 should not be reapplied.

4. CONCLUSION

For all the foregoing reasons, it is requested that the pending claims be deemed allowable.

Respectfully submitted,



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CLAIMS MARKED TO SHOW AMENDMENTS

1. (twice amended) A medicinal product for topical use for the promotion of wound healing, which comprises (a) thrombocytes or thrombocyte fragments, wherein said thrombocytes or thrombocyte fragments (i) contain growth factors and are capable of releasing the same over an extended period of time, (ii) have been prepared by a method selected from the group consisting of [(a)] lyophilization and [(b) deep] freezing; and (iii) have been subjected to a process [for] selected from the group consisting of virus partitioning and[/or] virus inactivation; and (b) a thrombocyte activating stimulus selected from the group consisting of collagen, thrombin, trypsin, ADP, serotonin and adrenalin.

2. (twice amended) A medicinal product according to claim 1, wherein [characterized in that] the content of thrombocytes or thrombocyte fragments is such that it corresponds to at least 10^4 thrombocytes per ml after reconstitution of the lyophilisate or thawing.

3. (twice amended) A medicinal product according to claim 1, [characterized in that] wherein the medicinal product comprises additional growth factors.

4. (twice amended) A medicinal product according to claim 1, [characterized in that] wherein the medicinal product comprises [biomaterials] a cross-linkable human protein selected from the group consisting of fibrinogen, fibronectin, blood coagulation factor XIII and collagen.

5. (amended) A medicinal product according to claim 4, [characterized in that] wherein the [biomaterials have] cross-linkable human protein has been subjected to a process [for] selected from the group consisting of virus partitioning and[/or] virus inactivation.

6. (twice amended) A medicinal product according to claim 4, [characterized in that] wherein the [biomaterials are] cross-linkable human protein is present in the lyophilized or [deep-]frozen state.

7. (twice amended) A medicinal product according to claim 4[, characterized in that tissue adhesive and/or collagen are provided as biomaterials]

wherein the cross-linkable human protein is fibrinogen and the thrombocyte activating stimulus is thrombin.

8. (amended) A medicinal product according to claim [7] 1, [characterized in that] further comprising a [the] tissue adhesive [is] composed of fibrinogen-containing proteins and wherein the thrombocyte activating stimulus is thrombin.

9. (twice amended) A medicinal product according to claim 4, [characterized in that] wherein the medicinal product additionally comprises a component selected from the group consisting of epithelial cells, [and/or] keratinocytes, [and/or] embryonic cells, [and/or] fetal cells, [and/or] liposomes and combinations thereof.

10. (twice amended) A method of promoting the healing of a wound in a subject, comprising (i) applying to the wound a composition comprising thrombocytes or thrombocyte fragments containing growth factors and capable of releasing the same over an extended period of time and (ii) applying to the wound a thrombocyte activating stimulus selected from the group consisting of collagen, thrombin, trypsin, ADP, serotonin and adrenalin.

12. (amended) A medicinal product according to claim 5, [characterized in that] wherein the [biomaterials are] cross-linkable human protein is present in the lyophilized or [deep-]frozen state.

13. (amended) A medicinal product according to claim 5, [characterized in that] wherein the cross-linkable human protein is fibrinogen and the thrombocyte activating stimulus is thrombin [tissue adhesive and/or collagen are provided as biomaterials].

14. (amended) A medicinal product according to claim 6, [characterized in that] wherein the cross-linkable human protein is fibrinogen and the thrombocyte activating stimulus is thrombin [tissue adhesive and/or collagen are provided as biomaterials].

15. (amended) A medicinal product according to claim 1 [13], [characterized in that the] further comprising a tissue adhesive [is] composed of fibrinogen-containing proteins and wherein the thrombocyte activating stimulus is

thrombin, and wherein the tissue adhesive and thrombin have been subjected to a process selected from the group consisting of virus partitioning and virus inactivation.

16. (amended) A medicinal product according to claim 1[14], [characterized in that the] further comprising a tissue adhesive [is] composed of fibrinogen-containing proteins and wherein the thrombocyte-activating stimulus is thrombin, and wherein the tissue adhesive and thrombin are present in the lyophilized or frozen state.

17. (twice amended) A medicinal product according to claim 5, [characterized in that] wherein the medicinal product additionally comprises a component selected from the group consisting of epithelial cells, [and/or] keratinocytes, [and/or] embryonic cells, [and/or] fetal cells, [and/or] liposomes and combinations thereof.

18. (twice amended) A medicinal product according to claim 6, [characterized in that] wherein the medicinal product additionally comprises a component selected from the group consisting of epithelial cells, [and/or] keratinocytes, [and/or] embryonic cells, [and/or] fetal cells, [and/or] liposomes and combinations thereof.

19. (twice amended) A medicinal product according to claim 7, [characterized in that] wherein the medicinal product additionally comprises a component selected from the group consisting of epithelial cells, [and/or] keratinocytes, [and/or] embryonic cells, [and/or] fetal cells, [and/or] liposomes and combinations thereof.

20. (twice amended) A medicinal product according to claim 8, [characterized in that] wherein the medicinal product additionally comprises a component selected from the group consisting of epithelial cells, [and/or] keratinocytes, [and/or] embryonic cells, [and/or] fetal cells, [and/or] liposomes and combinations thereof.